

TEXT SEARCHABLE DOCUMENT - 2011

Data Evaluation Record on the hydrolysis of clothianidin

PMRA Submission Number {.....}

EPA MRID Number 47483003

Data Requirement: PMRA Data Code:
EPA DP Barcode: 357014
OECD Data Point:
EPA Guideline: 835.2120

Test material:

Common name: Clothianidin.

Chemical name:

IUPAC name: (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine.
(E)-N-(2-chloro-1,3-thiazol-5-yl)methyl]-N-[oxido(oxo)hydrazono]methanedianiline.
Chloro-1,3-thiazol-5-yl)methyl]-N-{(E)-(methylamino)[oxido(oxo)hydrazono]methyl} amine.

CAS name: [C(E)]-N-[(2-chloro-5-thiazolyl)methyl]-N'-methyl-N''-nitroguanidine.

CAS No.: 210880-92-5 (formerly 205510-53-8).

Synonyms: C-1015, C-908, TI435, K-1142, TI-435, TI-435 50 WDG, TI-435 50WDG.

Smiles string: CNC(=N[N+](=O)O)NCc1cnc(Cl)s1 (Online SMILES Translator and Structure File Generator at <http://cactus.nci.nih.gov/services/translate/>).
[O-][N+](=O)N=C(NC1cnc(s1)Cl)NC.

Primary Reviewer: Moncie Wright
Cambridge Environmental

Signature:
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Final Reviewer: William P. Eckel
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Date: 01/24/2011

Company Code:
Active Code:
Use Site Category:
EPA PC Code: 044309

CITATION: Dominic, A.R., and E.L. Arthur. 2006. Clothianidin: Long-term hydrolytic degradation. Unpublished study performed by Bayer CropScience, Stillwell, Kansas; sponsored and submitted by Bayer CropScience, Research Triangle Park, North Carolina. Bayer CropScience Study No./Report No.: METIX051. Experiment started June 22, 2004, and completed August 18, 2005 (p. 6). Final report issued February 8, 2006.



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EXECUTIVE SUMMARY

The hydrolysis of [thiazole-2-¹⁴C]-labeled (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine (clothianidin; radiochemical purity $\geq 95.7\%$), at 0.3 mg a.i./L, was studied in sterile aqueous buffered (0.01M Tris) pH 7 solutions that were incubated in the dark at 10°C, 20°C, 30°C, 40°C, or 50°C for up to 368 days. The experiment was conducted in accordance with USEPA Pesticide Assessment Guidelines, Subdivision N §161-1 and in compliance with USEPA FIFRA GLP standards (40 CFR 160). The test system consisted of amber serum vials (20 mL volume) containing treated buffer solution (10 mL) that were sealed with Teflon-lined septa and crimp caps. Volatiles were not addressed. Samples were maintained in either temperature-controlled incubators (10 and 20°C samples) or in covered waterbaths (30, 40, and 50°C). Duplicate samples were collected from each treatment at the following intervals:

10°C: 0, 15, 34, 61, 91, 125, 181, 270, and 368 days;
20°C: 0, 13, 32, 60, 90, 120, and 180 days;
30°C: 0, 13, 32, 60, 90, and 120 days;
40°C: 0, 5, 7, 14, 34, and 61 days; and
50°C: 0, 4, 7, 13, 26, and 32 days.

Aliquots of the samples were analyzed without modification by LSC and HPLC. Samples were cochromatographed with unlabeled reference standards of clothianidin and its transformation products clothianidin desmethyl, clothianidin thiazolyl methylurea, and clothianidin thiazolyl urea (purities not reported). Identification of clothianidin was confirmed using a second HPLC method and LC-ESI/MS in positive ion mode.

During the study, the temperatures of the buffer solutions were 7.8-10.7°C (10°C), 19.0-19.6°C (20°C), 29.8-31.5°C (30°C), 40.1°C (40°C), and 49.9-50.1°C (50°C). The pH of the buffer solutions ranged from 6.66 to 7.27 across all temperatures. The buffer solutions were reported as sterile at test termination with the exception of a single replicate at day 90 in the 30°C test; no supporting data were provided.

Overall recoveries of [¹⁴C]residues averaged $99.3 \pm 2.1\%$ of the applied (range 92.0-102.0%) from the 10°C buffer solution, $99.8 \pm 1.7\%$ (range 96.6-103%) from the 20°C buffer solution, $99.3 \pm 1.3\%$ (range 97.3-101%) from the 30°C buffer solution, $98.9 \pm 1.8\%$ (range 94.1-101%) from the 40°C buffer solution and $99.0 \pm 0.9\%$ (range 97.4-100%) from the 50°C buffer solution. There was no pattern of loss of material over time from any of the buffer solutions.

Clothianidin was stable to relatively stable (half-life >3 years) at all temperatures. In the 10, 20, and 30°C solutions, a half-life could not be determined because the reviewer-calculated first order log/linear regression equations (Excel 2003) had a positive slope. In the 40 and 50°C solutions, clothianidin dissipated with log/linear half-lives of 1,732.9 (4.7 years) and 1,155.2 days (3.2 years), respectively. These half-lives are of highly uncertain value since they are extrapolated well beyond the duration of the experiments (61 and 32 days, respectively).

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In all test solutions, [^{14}C]clothianidin averaged 95.4-99.4% of the applied at the final sampling interval, which ranged from 32 days at 50°C to 368 days at 10°C. No major transformation products were isolated and no minor transformation products were identified in any samples. Volatiles were not addressed.

At 10°C, [^{14}C]clothianidin averaged 98.9% of the applied at time 0, 93.4-100.0% at 15-270 days posttreatment with no pattern of decline, and 98.4% at 368 days (study termination). No major transformation products were isolated and no minor transformation products were identified in any samples. Two unidentified HPLC peaks averaged 1.3% and 0.6% of the applied. Volatiles were not addressed.

At 20°C, [^{14}C]clothianidin averaged 99.4% of the applied at time 0, 96.9-100.5% at 13-120 days posttreatment with no pattern of decline, and 99.4% at 180 days (study termination). No major transformation products were isolated and no minor transformation products were identified in any samples. An unidentified HPLC peak averaged a maximum of 1.3% of the applied. Volatiles were not addressed.

At 30°C, [^{14}C]clothianidin averaged 99.4% of the applied at time 0, 96.2-99.9% at 13-90 days posttreatment with no pattern of decline, and 98.8% at 120 days (study termination). No major transformation products were isolated and no minor transformation products were identified in any samples. Two unidentified HPLC peaks averaged maximums of 1.2% and 0.5% of the applied. Volatiles were not addressed.

At 40°C, [^{14}C]clothianidin averaged 98.9% of the applied at time 0, 97.3-99.2% with no pattern of decline at 5-34 days posttreatment, and 95.4% at 61 days (study termination). No major transformation products were isolated and no minor transformation products were identified in any samples. An unidentified HPLC peak averaged a maximum of 1.4% of the applied. Volatiles were not addressed.

At 50°C, [^{14}C]clothianidin averaged 99.4% of the applied at time 0, 96.8-99.3% with no pattern of decline at 4-26 days posttreatment, and 97.2% at 32 days (study termination). No major transformation products were isolated and no minor transformation products were identified in any samples. An unidentified HPLC peak averaged a maximum of 1.4% of the applied. Volatiles were not addressed.

Since clothianidin was stable to relatively stable (<5% dissipation) during the study, a transformation pathway could not be developed.

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RESULTS SYNOPSIS:

pH 7	Half-life (days)	Major and minor transformation products
10°C	Stable	None
20°C	Stable	None
30°C	Stable	None
40°C	1,732.9	None
50°C	1,155.2	None

Study Acceptability: This study is classified as acceptable. No significant deviations from good scientific practices were noted. The experiments were conducted in pH 7 Tris buffer only. The study authors stated that the study was requested by PMRA to address the hydrolysis of clothianidin in groundwater.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was reportedly conducted in accordance with USEPA Pesticide Assessment Guidelines, Subdivision N §161-1, and Canadian PMRA DACO Number 8.2.3.2 (pp. 1, 14, 25-26). However, the study was specifically designed to address concerns about the long-term hydrolysis in groundwater and experiments were conducted only at pH 7 (p. 14).

COMPLIANCE: This study was conducted in compliance with USEPA FIFRA GLP standards (40 CFR part 160, 1989). Signed and dated Data Confidentiality, GLP, Quality Assurance, and Certificate of Authenticity (Certification) statements were provided (pp. 2-5).

A. MATERIALS:

1. Test Materials [Thiazole-2-¹⁴C]clothianidin (p. 15, Figure 1, p. 40).

Chemical Structure: See DER Attachment 1.

Description: Technical grade.

Purity: Radiochemical purity: 95.7% (Vial C-1015; pp. 15, 17).
98.9% (Vial C-908).

Lot No. Not reported.

Analytical purity: Not reported.

Specific activity: 26.4 mCi/mMole (p. 15).

Location of the radiolabel: Labeled on the 2 Carbon (chlorine carbon) in the thiazole moiety (p. 15, Figure 1, p. 40).

Storage conditions of test chemicals: The technical grade test materials were stored frozen in a solution of acetonitrile (p. 15).

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Physico-chemical properties of clothianidin.

Parameter	Value	Comment
Molecular weight (g/Mol)	249.7	
Molecular formula	Not reported.	
Water Solubility (g/L)	0.327	At 20°C.
Vapor Pressure (Pa)	1.3×10^{-10} 3.8×10^{-11}	At 25°C. At 20°C (extrapolated).
UV Absorption	Not reported.	
pKa	11.09	At 20°C.
log K _{ow}	0.7	At 25°C.
Stability of compound at room temperature, if provided	Not reported.	

Data were obtained from p. 15 and Figure 1, p. 40 of the study report. The molecular formula was obtained from DER Attachment 1.

2. Buffer Solution: Buffer solutions were prepared as follows:

Table 1: Description of buffer solutions.

pH	Type and molarity of buffer	Composition
7	0.01M Tris	2.42 g of tris(hydroxymethyl)aminomethane were dissolved in 2 L of Milli-Q water, and 1.5 mL of 10N HCl was added. The pH of the solution was adjusted to pH 7 using 1.4 mL of 1M NaOH.

Data obtained from p. 16 of the study report.

B. EXPERIMENTAL CONDITIONS

1. Preliminary Study: No preliminary studies were described.

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2. Experimental conditions

Table 2: Experimental parameters

Parameters		Details
Duration of study		10°C: 368 days. 20°C: 180 days. 30°C: 120 days. 40°C: 61 days. 50°C: 32 days.
Test concentrations	Nominal:	0.3 mg a.i./L.
	Measured:	0.3 mg a.i./L.
No. of replications		Duplicate samples from each temperature were collected at each sampling interval.
Preparation of test medium	Volume used/treatment	86-90 µL/10 mL buffer.
	Method of sterilization	The buffer solutions were autoclaved (>200°F).
	Co-solvent	Acetonitrile, ca. 0.9% by volume.
Test apparatus (type/material/volume)		The test system consisted of amber serum vials (20 mL volume) containing treated buffer solution (10 mL) that were sealed with Teflon-lined septa and crimp caps. Samples were incubated in temperature-controlled incubators (10 and 20°C samples) or in covered waterbaths (30, 40, and 50°C). The test vials are illustrated in Figure 3, p. 43.
Details of traps for volatile, if any		Volatile traps were not used.
If no traps were used, is the test system closed/open?		Closed.
Is there any indication of the test material adsorbing to the walls of the test apparatus?		None.
Experimental conditions	Temperature (°C):	10°C: 7.8-10.7°C (mean 9.3°C). 20°C: 19.0-19.6°C (mean 19.3°C). 30°C: 29.8-31.5°C (mean 30.0°C). 40°C: 40.1°C (mean 40.1°C). 50°C: 49.9-50.1°C (mean 50.1°C).
	Lighting:	Dark. p. 18
	pH ranges:	10°C: 6.80-7.16. 20°C: 6.66-6.91. 30°C: 6.66-7.17. 40°C: 6.90-7.27. 50°C: 6.66-7.06.
Other details, if any		None.

Data were obtained from pp. 14, 16-19; Table 1, p. 27; Table 3, p. 29; Figure 3, p. 43 and Figure 9, pp. 51-52 of the study report.

3. Supplementary Experiments: To aid in metabolite identification, additional buffered samples were prepared and treated at 3.0 mg a.i./L, which was 10x the application rate used in the definitive experiments (pp. 17-18). Aliquots (75-90 µL) of these stock solutions were added to each test system for a final test concentration of 3.0 mg/L.

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4. Sampling:

Table 3: Sampling details.

Criteria	Details
Sampling intervals	10°C: 0, 15, 34, 61, 91, 125, 181, 270, and 368 days. 20°C: 0, 13, 32, 60, 90, 120, and 180 days. 30°C: 0, 13, 32, 60, 90, and 120 days. 40°C: 0, 5, 7, 14, 34, and 61 days. 50°C: 0, 4, 7, 13, 26, and 32 days.
Sampling method	Two vials of treated buffer were collected from each temperature treatment at each sampling interval.
Method of collection of CO ₂ and organic volatile compounds	Volatiles were not collected.
Sampling intervals/times for: pH measurement: Sterility check:	At each sampling interval. At each sampling interval.
Sample storage before analysis	Samples were typically analyzed on the day of sampling. The maximum storage duration before analysis was 1 day. Samples were stored at <-19.8°C (mean) prior to analysis.
Other observation, if any:	None.

Data were obtained from p. 19 and Table 2, p. 28 of the study report.

C. ANALYTICAL METHODS

Extraction/clean up/concentration methods: Samples were analyzed as collected, without manipulation or modification (p. 19).

Volatile residue determination: Volatiles were not trapped.

Total ¹⁴C measurement: Aliquots of the treated buffer solutions were analyzed for total [¹⁴C]residues using LSC (p. 19; Figure 5, p. 45).

Derivatization method, if used: A derivatization method was not employed.

Identification and quantification of parent compound: Aliquots of the buffer solutions were analyzed directly by HPLC Method 1 under the following conditions: YMC ODS-AQ SN 042544567 column, gradient mobile phase consisting of (A) 1% phosphoric acid in Milli-Q water and (B) acetonitrile [percent A:B (v:v) at 0 minutes, 100:0; 1 minute, 100:0; 26 minutes, 0:90; 27 minutes, 0:100; 30 minutes, 0:100], flow rate 1 mL/minute, with UV (254 nm) and radioflow detection (pp. 19-20). Clothianidin was identified by comparison to an unlabeled reference standard (Rt ca. 18 minutes; purity not reported; pp. 20, 24; Figure 1, p. 40; Figure 6A-D, pp. 46-47). Column recoveries were monitored by collecting the HPLC effluent and comparing LSC results to the expected radioactivity injected onto the column (p. 21).

To confirm the analytical results, samples were also analyzed by HPLC Method 2 under the following conditions: Phenomenex Aqua 5 µ, C18 125A (250 x 4.6) column, gradient mobile

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phase consisting of (A) 0.1% formic acid in Milli-Q water and (B) acetonitrile [percent A:B (v:v) at 0 minutes, 100:0; 3 minutes, 100:0; 25 minutes, 0:95; 28 minutes, 0:95; 30 minutes, 100:0], flow rate 1 mL/minute, with UV (254 nm) and radioflow detection (pp. 19-20). Clothianidin was identified by comparison to an unlabeled reference standard (Rt *ca.* 18.8 minutes; purity not reported; pp. 20, 24; Figure 1, p. 40; Figure 6E, p. 46; Figure 7, p. 48).

The identity of clothianidin was also confirmed using LC-ESI/MS in positive ion mode (pp. 21, 24).

Identification and quantification of transformation products: Transformation products were separated and quantified using HPLC as described for the parent (pp. 19-20). The following reference compounds were available for use:

Common name	IUPAC name	Purity	Rt (minutes)
Desmethyl	N-[(2-Chloro-1,3-thiazol-5-yl)methyl][oxido(oxo)hydrazono]methanediamine	--	<i>ca.</i> 17.2
Thiazolyl methylurea	1-(2-Chlorothiazol-5-ylmethyl)-3-methylurea	--	<i>ca.</i> 16.3
Thiazolyl urea	N-[(2-Chloro-1,3-thiazol-5-yl)methyl]urea	--	<i>ca.</i> 14.3

Data obtained from Figure 1, pp. 40-41 and Figure 7, p. 48 in the study report.

Detection limits (LOD, LOQ) for the parent compound: For LSC, the minimum sensitivity was 2x background, or 0.03% of the applied (Appendix 2, p. 57).

Detection limits for HPLC are uncertain. The Limit of Quantification is reported to be 1.5% of the applied in Appendices 4-8 (pp. 59-63) and 3.0% (twice the Limit of Detection) in the text (page 24).

Detection limits (LOD, LOQ) for the transformation products: The LOD and LOQ were the same as for the parent.

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS: During the study, the temperatures of the buffer solutions were 7.8-10.7°C (10°C), 19.0-19.6°C (20°C), 29.8-31.5°C (30°C), 40.1°C (40°C), and 49.9-50.1°C (50°C; Figure 9, pp. 51-52). The pH of the buffer solutions ranged from 6.66 to 7.27 across all temperatures (Table 3, p. 29). The buffer solutions were reported as sterile at test termination with the exception of a single replicate at day 90 in the 30°C test; no supporting data were provided (p. 23).

B. MASS BALANCE: Overall recoveries of [¹⁴C]residues averaged 99.3 ± 2.1% of the applied (range 92.0-102.0%) from the 10°C buffer solution, 99.8 ± 1.7% of the applied (range 96.6-103%) from the 20°C buffer solution, 99.3 ± 1.3% of the applied (range 97.3-101%) from the 30°C buffer solution, 98.9 ± 1.8% of the applied (range 94.1-101%) from the 40°C buffer

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solution and $99.0 \pm 0.9\%$ (range 97.4-100%) from the 50°C buffer solution (Tables 4-8, pp. 30-34; DER Attachment 2). There was no pattern of loss of material over time from any of the buffer solutions.

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Table 4a: Hydrolysis of [^{14}C]clothianidin, expressed as percentage of the applied radioactivity (mean \pm s.d., n = 2), at pH 7 and 10°C.

Compound	Sampling times (days)								
	0	15	34	61	91	125	181	270	368
Clothianidin	98.9 \pm 0.1	97.7 \pm 0.4	97.7 \pm 1.3	93.4 \pm 5.3	99.4 \pm 0.1	98.3 \pm 0.1	100.0 \pm 0.1	98.8 \pm 0.0	98.4 \pm 0.1
Unknown 1 (A) ¹	1.2 \pm 0.1	1.1 \pm 0.0	1.3 \pm 1.0	1.3 \pm 0.0	1.2 \pm 0.0	1.2 \pm 0.1	1.2 \pm 0.6	0.0 \pm 0.6	0.5 \pm 0.8
Unknown 2 (B) ¹	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0	0.6 \pm 0.0	0.0 \pm 0.0	0.3 \pm 0.4	0.0 \pm 0.0	0.0 \pm 0.0	0.3 \pm 0.4
CO ₂	Volatiles were not collected.								
Volatile organics	Volatiles were not collected.								
Total Recovery	100.0 \pm 0.0	98.7 \pm 0.3	99.0 \pm 0.4	95.3 \pm 4.7	101.0 \pm 0.0	99.8 \pm 0.3	101.5 \pm 0.7	98.8 \pm 0.0	99.2 \pm 1.0

Means and standard deviations, except for unknown compounds, were calculated by the reviewer using data obtained from Table 4, p. 30, Table 9, p. 35, and Appendix 4, p. 59 in the study report (DER Attachment 2).

¹ With the exception of Unknown 1 Days 34 and 61 Replicate 2 and Day 181 Replicate 1, the concentrations of Unknowns 1 and 2 were below the Limit of Quantification (1.5%) at all sampling intervals (Appendix 4, p. 50).

Table 4b: Hydrolysis of [^{14}C]clothianidin, expressed as percentage of the applied radioactivity (mean \pm s.d., n = 2), at pH 7 and 20°C.

Compound	Sampling times (days)						
	0	13	32	60	90	120	180
Clothianidin	99.4 \pm 0.9	96.9 \pm 1.7	98.0 \pm 0.5	98.4 \pm 0.1	100.5 \pm 0.7	99.6 \pm 3.5	99.4 \pm 3.7
Unknown 1 (A) ¹	0.5 \pm 0.7	0.9 \pm 0.0	0.6 \pm 0.9	1.2 \pm 0.1	1.3 \pm 0.5	0.9 \pm 0.2	1.2 \pm 0.1
CO ₂	Volatiles were not collected.						
Volatile organics	Volatiles were not collected.						
Total Recovery	99.9 \pm 0.1	97.8 \pm 1.6	98.6 \pm 0.4	99.6 \pm 0.1	102.0 \pm 0.0	100.5 \pm 3.6	100.0 \pm 0.0

Means and standard deviations, except for unknown compounds, were calculated by the reviewer using data obtained from Table 5, p. 31, Table 10, p. 36, and Appendix 5, p. 60 in the study report (DER Attachment 2).

¹ Unknown 1 was below the Limit of Quantification (1.5%) at all sampling intervals (Appendix 5, p. 60).

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Table 4c: Hydrolysis of [¹⁴C]clothianidin, expressed as percentage of the applied radioactivity (mean ± s.d., n = 2), at pH 7 and 30°C.

Compound	Sampling times (days)					
	0	13	32	60	90	120
Clothianidin	99.4 ± 0.9	96.2 ± 0.9	97.0 ± 0.5	98.6 ± 0.1	99.9 ± 0.6	98.8 ± 0.7
Unknown 1 (A) ¹	0.5 ± 0.7	1.0 ± 0.3	1.0 ± 0.0	1.1 ± 0.1	1.1 ± 0.1	1.2 ± 0.1
Unknown 2 (B) ¹	0.0 ± 0.0	0.5 ± 0.7	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
CO ₂	Volatiles were not collected.					
Volatile organics	Volatiles were not collected.					
Total Recovery	99.9 ± 0.1	97.6 ± 0.4	98.0 ± 0.5	99.8 ± 0.2	101.0 ± 0.0	99.8 ± 0.4

Means and standard deviations, except for unknown compounds, were calculated by the reviewer using data obtained from Table 6, p. 32, Table 11, p. 37, and Appendix 6, p. 61 in the study report (DER Attachment 2).

1 Unknowns 1 and 2 were below the Limit of Quantification (1.5%) at all sampling intervals (Appendix 6, p. 61).

Table 4d: Hydrolysis of [¹⁴C]clothianidin, expressed as percentage of the applied radioactivity (mean ± s.d., n = 2), at pH 7 and 40°C.

Compound	Sampling times (days)					
	0	5	7	14	34	61
Clothianidin	98.9 ± 0.1	97.9 ± 1.1	97.3 ± 1.0	98.0 ± 1.0	99.2 ± 0.2	95.4 ± 3.2
Unknown 1 (A)	1.2 ± 0.1	1.0 ± 0.2	1.1 ± 0.0	1.3 ± 0.2	1.4 ± 0.0	1.2 ± 0.2
CO ₂	Volatiles were not collected.					
Volatile organics	Volatiles were not collected.					
Total Recovery	100.0 ± 0.0	99.0 ± 0.9	98.4 ± 1.0	99.3 ± 0.8	100.5 ± 0.7	96.6 ± 3.5

Means and standard deviations, except for unknown compounds, were calculated by the reviewer using data obtained from Table 7, p. 33, Table 12, p. 38, and Appendix 7, p. 62 in the study report (DER Attachment 2).

1 Unknown 1 was below the Limit of Quantification (1.5%) at all sampling intervals (Appendix 7, p. 62).

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Table 4e: Hydrolysis of [^{14}C]clothianidin, expressed as percentage of the applied radioactivity (mean \pm s.d., n = 2), at pH 7 and 50°C.

Compound	Sampling times (days)					
	0	4	7	13	26	32
Clothianidin	99.4 \pm 0.9	99.3 \pm 0.9	97.7 \pm 0.4	96.8 \pm 1.0	97.3 \pm 1.0	97.2 \pm 1.3
Unknown 1 (A) ¹	0.5 \pm 0.7	0.6 \pm 0.8	1.3 \pm 0.4	1.2 \pm 0.2	1.3 \pm 0.1	1.4 \pm 0.1
CO ₂	Volatiles were not collected.					
Volatile organics	Volatiles were not collected.					
Total Recovery	99.9 \pm 0.1	99.9 \pm 0.1	99.0 \pm 0.7	98.0 \pm 0.8	98.5 \pm 0.8	98.7 \pm 1.2

Means and standard deviations, except for unknown compounds, were calculated by the reviewer using data obtained from Table 8, p. 34, Table 13, p. 39, and Appendix 8, p. 63 in the study report (DER Attachment 2).

1 With the exception of Day 7 Replicate 2 and Day 32 Replicate 1, Unknown 1 was below the Limit of Quantification (1.5%) at all sampling intervals (Appendix 8, p. 63).

C. TRANSFORMATION OF PARENT COMPOUND: At 10°C, [^{14}C]clothianidin averaged average of 93.4-100.0% of the applied during the study with no obvious pattern of decline (DER Attachment 2).

At 20°C, [^{14}C]clothianidin averaged 96.9-100.5% of the applied during the study with no obvious pattern of decline (DER Attachment 2).

At 30°C, [^{14}C]clothianidin averaged 96.2-99.9% of the applied during the study with no obvious pattern of decline (DER Attachment 2).

At 40°C, [^{14}C]clothianidin averaged 98.9% of the applied at time 0, 97.3-99.2% with no pattern of decline at 5-34 days posttreatment, and 95.4% at 61 days (study termination; DER Attachment 2).

At 50°C, [^{14}C]clothianidin averaged 99.4% of the applied at time 0, 96.8-99.3% with no pattern of decline at 4-26 days posttreatment, and 97.2% at 32 days (study termination; DER Attachment 2).

HALF-LIVES/DT50/DT90: Clothianidin was stable to relatively stable (half-life >3 years) at all temperatures (DER Attachment 2). In the 10, 20, and 30°C solutions, a half-life could not be estimated because the reviewer-calculated first order log/linear regression equations (Excel 2003) had a positive slope. In the 40 and 50°C solutions, clothianidin dissipated with log/linear half-lives of 1,732.9 (4.7 years) and 1,155.2 days (3.2 years), respectively. These half-lives are of highly uncertain value since they are extrapolated well beyond the duration of the experiments (61 and 32 days, respectively).

The study authors did not calculate half-lives for any sample set.

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Half-lives/DT50/DT90

pH 7	First order linear ¹			Observed DT50	Observed DT90
	Half-life/DT50 (days)	Regression equation	r ²		
10°C	Stable, positive regression slope.			--	--
20°C	Stable, positive regression slope.			--	--
30°C	Stable, positive regression slope.			--	--
40°C	1,732.9	y = -0.0004x + 4.5901	0.2292	>61 days	>61 days
50°C	1,155.2	y = -0.0006x + 4.5929	0.3672	>32 days	>32 days

¹ Determined by the reviewer using Excel 2003 (linear, first-order) regression analysis and all data points from Appendices 4-8, pp. 59-63 of the study report (DER Attachment 2).

TRANSFORMATION PRODUCTS: No major transformation products were isolated and no minor transformation products were identified in any samples (Tables 9-13, pp. 35-39). Two HPLC peaks were quantified at averages of ≤1.4% of the applied in all samples and at all temperatures.

Table 5: Chemical names and CAS numbers for the transformation products of clothianidin.

Applicants Code Name	CAS Number	Chemical Name	Chemical Formula	MW (g/mol)	Smiles String
No transformation products were identified.					

VOLATILIZATION: Volatiles were not addressed.

TRANSFORMATION PATHWAY: A transformation pathway was not provided. Based on the study results, clothianidin is stable to hydrolysis under neutral conditions.

D. SUPPLEMENTARY EXPERIMENT-RESULTS: The study authors did not report whether the high dose samples were analyzed.

III. STUDY DEFICIENCIES

1. The five experiments were conducted in pH 7 Tris buffer only (p. 16). The study authors stated that the study was requested by PMRA "...to address the hydrolysis of clothianidin in groundwater, based on predicted concentrations from groundwater exposure modeling and evaluating the corn and canola seed treatment uses" (pp. 14-15).
2. Presumably for HPLC, the Limit of Quantification is reported to be 1.5% of the applied in the footnote to Appendices 4-8 (pp. 59-63). However, in the text (p. 24), the Limit of Detection is reported to be 1.5% of the applied and the Limit of Quantification to be 3.0%. The reviewer believes that it is most likely that 1.5% is the Limit of Quantification because in Tables 9-13 (pp. 35-39) the study authors report averaged concentrations for Unknowns 1 and 2 that are as low as 0.3%.

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3. Volatiles were not addressed. Since the material balances are complete for the duration of the study and the samples remained sterile during the study, failure to report this information does not affect the interpretation of the study results.

IV. REVIEWER'S COMMENTS

1. The study authors stated that the application rate used in this study was the same rate that was used in a previous clothianidin hydrolysis study, and was concentrated enough to allow for identification of transformation products (p. 15)
2. The study authors reported means and standard deviations for Unknowns 1 and 2 in Tables 9-13 (pp. 35-39). However, in Appendices 4-8 (pp. 59-63), concentration data for individual samples is most often reported as <LOQ (less than the Limit of Quantification).

V. REFERENCES

1. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate, Section 161-1. Hydrolysis studies. Office of Pesticide and Toxic Substances, Washington, DC. EPA 540/9-82-021.
2. U.S. Environmental Protection Agency. 1989. FIFRA Accelerated Reregistration, Phase 3 Technical Guidance. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 540/09-90-078.
3. U.S. Environmental Protection Agency. 1993. Pesticide Registration Rejection Rate Analysis - Environmental Fate. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 738-R-93-010.

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Attachment 1: Structure of Parent Compound and Transformation Products

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Clothianidin [C-1015, C-908, TI435, K-1142, TI-435, TI-435 50 WDG, TI-435 50WDG]

IUPAC Name: (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine.
(E)-N-(2-chloro-1,3-thiazol-5-yl)methyl]-N-[oxido(oxo)hydrazono]methanediamine.
Chloro-1,3-thiazol-5-yl)methyl]-N-{(E)-(methylamino)[oxido(oxo)hydrazono]methyl} amine.

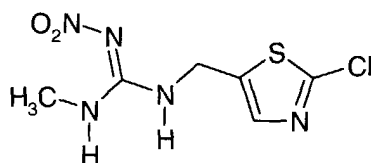
CAS Name: [C(E)]-N-[(2-chloro-5-thiazolyl)methyl]-N'-methyl-N''-nitroguanidine.

CAS Number: 210880-92-5 (formerly 205510-53-8).

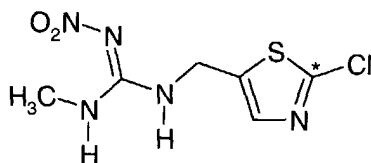
SMILES String: CNC(=N[N+](=O)O)NCc1cnc(Cl)s1 (Online SMILES Translator and Structure File Generator at <http://cactus.nci.nih.gov/services/translate/>).
[O-][N+](=O)N=C(NC)NCc1cnc(s1)Cl)NC.

Empirical formula: C₆H₈ClN₅O₂S **Molecular formula:** C₆H₈ClN₅O₂S

Unlabeled



[Thiazole-2-¹⁴C]Clothianidin



* = Location of the radiolabel.

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Identified Compounds

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Clothianidin [C-1015, C-908, TI435, K-1142, TI-435, TI-435 50 WDG, TI-435 50WDG]

IUPAC Name: (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine.

(E)-N-(2-chloro-1,3-thiazol-5-yl)methyl]-N-

[oxido(oxo)hydrazono]methanediamine.

Chloro-1,3-thiazol-5-yl)methyl]-N-{(E)-

(methylamino)[oxido(oxo)hydrazono]methyl} amine.

CAS Name: [C(E)]-N-[(2-chloro-5-thiazolyl)methyl]-N'-methyl-N''-nitroguanidine.

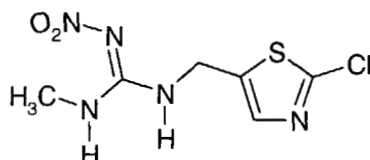
CAS Number: 210880-92-5 (formerly 205510-53-8).

SMILES String: CNC(=N[N+](=O)O)NCc1cnc(Cl)s1 (Online SMILES Translator and Structure File Generator at <http://cactus.nci.nih.gov/services/translate/>).

[O-][N+](=O)N=C(NC)NCc1cnc(s1)Cl)NC.

Empirical formula: C₆H₈ClN₅O₂S

Molecular formula: C₆H₈ClN₅O₂S



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Unidentified Reference Compounds

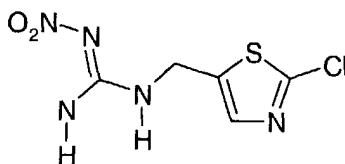
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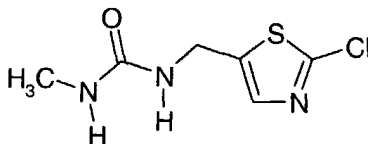
Desmethyl [TZNG, K-1177]

IUPAC Name: N-[(2-chloro-1,3-thiazol-5-yl)methyl][oxido(oxo)hydrazono]methanedianiline.
CAS Name: N-[(2-chloro-5-thiazolyl)methyl]-N'-nitroguanidine.
CAS Number: 135018-15-4.



Thiazolyl methylurea [TZMU, K-1178]

IUPAC Name: 1-(2-Chlorothiazol-5-ylmethyl)-3-methylurea.
CAS Name: N-[(2-Chloro-1,3-thiazolyl-5-yl)methyl]-N'-methylurea.
CAS Number: 634192-72-6.



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Thiazolyl Urea [TZU, K-1192]

IUPAC Name: N-[(2-Chloro-1,3-thiazol-5-yl)methyl]urea.

CAS Name: [(2-Chloro-5-thiazolyl)methyl]urea.

CAS Number: Not reported.

